CONFIDENTIAL

INVENTION DISCLOSURE FORM

(Directions for filling out your Idea Memorandum are at the end of this document)

Title:	Closed-loop control of a medical device using chemical biosensors

General Information

Invention Disclosure Form Submitted by: W. Rohr, A. Dextradeur, D. Konieczynski

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Dates		*Previous Disclosure(s)*
Invention/Discovery Conception	[redacted]	*When, how and to whom* has this been disclosed outside of J&J: No outside disclosure
First Written Description:	[redacted]	
Reduction to Practice:		Were disclosures made in confidence? N/A
Implementation Date:		
Market Release Date:		Where are records filed? N/A
First Offer for Sale:		

Closest Related Prior Art Reviewed

Patents:

1. US 4,889,407 Markle, "Optical waveguide sensor and method of making same" (Biomedical Sensors Ltd.)
2. US 5,396,988 Markle, "Multi-parameter sensor apparatus" (Biomedical Sensors Ltd.)
3. US 5,511,547 Markle, "Solid state sensors" (Biomedical Sensors Ltd.)
4. US 5,676,145 Bar-Lavie, "Cerebral hemodynamic monitoring system" (U. Md. Baltimore)
5. US 5,720,720 Laske, "Convection-enhanced drug delivery" (US DHHS)
6. US 6,016,449 Fischell, "System for treatment of neurological disorders" (NeuroPace, Inc.)
7. US 5,978,702 Ward, "Techniques of treating epilepsy by brain stimulation and drug infusion" (Medtronic)
8. US 5,711,316 Elsberry, "Method of treating movement disorders by brain infusion" (Medtronic)
9. US 5,735,814 Elsberry, "Techniques of treating neurodegenerative disorders by brain infusion" (Medtronic)
10. US 5,782,798 Rise, "Techniques for treating eating disorders by brain stimulation and drug infusion" (Medtronic)
11. US 5,792,212 Weijand, "Nerve evoked potential measurement system using chaotic sequences for noise rejection" (Medtronic)
12. US 5,474,552 Palti, "Implantable drug delivery pump" (CB-Carmel Biotechnology Ltd.)

Other:

1. RR Lonser, N Gogate, PF Morrison, JD Wood, EH Oldfield, "Direct convective delivery of macromolecules to the spinal cord," J Neurosurg, 89: 616-622, 1998.
2. MY Chen, RR Lonser, PF Morrison, LS Governale, EH Oldfield, "Variables affecting convection-enhanced delivery to the striatum: a systematic examination of rate of infusion, cannula size, infusate concentration, and tissue-cannula sealing time," J Neurosurg, 90: 315-320, 1999.
3. *Medical Instrumentation: Application and Design*, 2nd Edition, JG Webster, Ed., John Wiley & Sons, New York, 1995.
4. *The Biomedical Engineering Handbook*, JD Bronzino, Ed., CRC Press, New York, 1995.
5. *Principles of Neural Science*, 3rd Edition, ER Kanel, JH Schwartz, TM Jessell, Elsevier Science Publishing Company, New York, 1991.

DISCLOSURE DESCRIPTION

ABSTRACT –

This memoranda discloses an invention which uses biosensors to detect biochemical events for closed-loop feedback control of medical devices used to treat disorders of the central nervous system.

This invention is an improv ment over present technology because it bases closed-loop feedback control on the detection of biochemical events rather than electrical events.

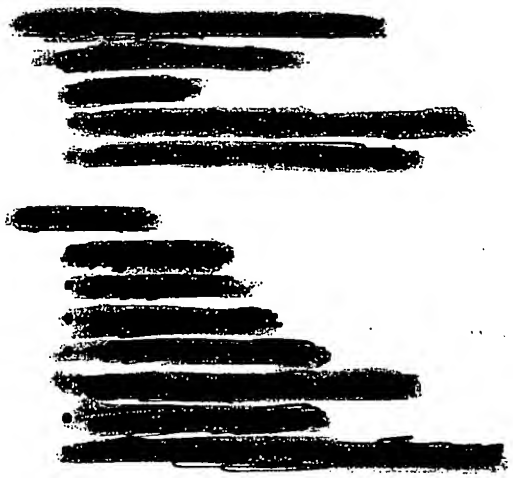
Biochemical events are directly related to the underlying disorder, whereas electrical (biopotential) events are secondary phenomena to the underlying disorder. By detecting biochemical events, it is possible to improve response time, and to improve therapeutic precision (e.g. multiple drugs, electrical stimulation).

The present invention offers additional therapeutic advantages. A preferred embodiment utilizes optical biosensors consisting of coated optic fibers. Using that technology, patient safety is enhanced both by minimizing patient exposure to electrical circuitry and by reducing device power requirements. A further advantage is that unlike electrode-based biopotential sensors, which typically require multiple leads to sense electric potentials, optical sensors are self-contained and do not require multiple lead placement.

DESCRIPTION OF THE PROBLEM THIS INVENTION SOLVES –

- Precise control of implantable medical device
- Detection of biochemical events – directly related to underlying disorder of CNS
- Preferred embodiment – optical based sensors
- Optical sensors enhance patient safety by eliminating patient electric contact, reduce power requirements
- Optical sensors do not require multiple site placement for detection

DESCRIPTION OF HOW OTHERS HAVE ATTEMPTED TO SOLVE THIS PROBLEM AND WHY THEIR SOLUTIONS ARE NOT OPTIMAL -



BROAD SUMMARY OF THE INVENTION -

Apparatus and methods for closed-loop feedback control of a drug infusion pump for treatment of disorders of the CNS or PNS. Closed-loop control is based on measurements from biosensors that sense the infused drugs or the metabolites or physiologic chemicals that derive from the administration of these drugs.

DETAILED DESCRIPTION OF THE INVENTION (Provide flow charts, drawings, etc. as appropriate.) -

- Integrate biosensors with closed-loop control of implantable medical devices used to treat disorders of the central nervous system. Biosensors measure biochemical events directly through several technologies: gas, electrochemical, bioanalytic, photometric, and other physical/chemical processes.
- Method and apparatus of placing biosensors at locations of the CNS remote from the infusion site of the drug pump. The sensors detect the agent delivered via the infusion system, to base control of infusion pump based on perfusion of agent at targeted sites.
- Method and apparatus of placing biosensors at various locations of the CNS (both in proximity of the infusion site as well as remote from the infusion site) to detect the *metabolite* of the infused agent(s).
- Method and apparatus of placing biosensors at various locations of the CNS (both in proximity of the infusion site as well as remote from the infusion site) to detect *physiologic chemicals* that result from the infused agent(s).

LIST UNIQUE ADVANTAGE(s) REALIZED BY THE INVENTION -

This invention has the following advantages:

- Offers improved, direct control of the perfusion of drugs within the CNS using closed-loop feedback.
- Apparatus detects biochemical signals that are directly related to the infused drugs, metabolites, or physiologic chemicals. This is a more direct measurement of the therapy and its effect than measurement of secondary electrical effects via electrodes.
- Patient safety is enhanced both by minimizing patient exposure to electrical circuitry and by reducing device power requirements.
- Optical sensors are self-contained and do not require multiple lead placement, unlike electrode-based biopotential sensors, which typically require multiple leads to sense electric potentials.

INVENTOR(s) INFORMATION

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APPLICABLE FRANCHISE TEAM(s)

☐ Instruments ☐ Hydrocephalus ☐ Cranial Products ☒ Neuro Trauma ☒ Strategic Planning

WITNESS SIGNATURE

"The foregoing memorandum consisting of 3 *pages was read and understood by me"*

Witness Signature & Date: Dayton 9-20 [redacted]

Based upon a physician's knowledge of a disease state, the dosage requirement for each of the measured (sensed) metabolite is established. The physician would control the setting and any future adjustments based upon the information received from the multiparameter sensor. These sensors can be located not only directly at the site (locally) of the event - disease/trauma - but also anywhere in the immediate area (regionally) or remote from this site in order to sense the "global" effect of treatment regime.

The sensors will be specifically designed to detect a particular event that is directly related the underlying disorder. An example of this would be for Parkinson's Disease. The nervous system uses the chemicals dopamine and acetylcholine to transmit signals that control muscle movements in the body. Dopamine is produced in the substantia nigra in the brain and then sent to the striatum. Equal amounts of dopamine and acetylcholine in the striatum are essential for creating smooth, coordinated muscle movement. Once in the striatum, these neurotransmitters are released and help direct muscle activity. Parkinson's occurs when cells that produce dopamine die off. Without dopamine, the activity of other related brain areas can be substantially altered. A sensor detecting this event, or lack thereof, would trigger introduction of a drug like Levodopa, which the brain converts to dopamine, and can help diminish the symptoms of the disease at an early stage. The sensor could detect the levels of dopamine and acetylcholine, these signals are sent to the controller, where governing parameters are set, and trigger an automatic response. When concentrations of the infused drugs or sensed metabolites were too high or too low, the device would respond accordingly.

Another dopamine agonist found in the literature is Pramipexole. Pramipexole has shown clinical efficacy in treating Parkinson symptoms at an early stage.

It's envisioned that antagonists can be used to actually stop cell death or blocking its nervous receptor leading to progression of an undesirable event.

The multiparmeter in-vivo sensor will detect particular chemical characteristics and reactions of a particular living system or biological substance. An example of an optic based multi-parameter sensor is disclosed in US 5,596,988.

A controller would detect the non-electrical signal produced by the metabolite and determine if the concentration of the metabolite is within the predetermined range. The system may be telemetrically altered to adjust the desired the state or condition within a physicians predetermine range which will be maintained until the controller is adjusted by the physician.

US 5,474,551 describes a similar method but the sensor is implanted in the body tissue or fluids of a person and generates an electrical signal based on the electrical activity of the living cells. The primary constituent is glucose.